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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,218	01/28/2002	Arne Holmgren	P21480	8453

7055 7590 02/26/2007

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EXAMINER	
KUMAR, SHAILENDRA	
ART UNIT	PAPER NUMBER
1621	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	02/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 02/26/2007.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	09/926,218	HOLMGREN ET AL.	
	Examiner	Art Unit	
	SHAILENDRA -. KUMAR	1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-19 and 26-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-19 and 26-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to applicants' communication filed on 11/30/06. Claims 13-19 and newly added claims 26-28 are pending in this application. Claims 20-25 have been canceled.

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on 11/30/06 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Objections

2. Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This claim depends from the claim 17, which is following claim 16. This claim needs to depend from the previous claim rather than the following claim.

Claim Rejections - 35 USC § 103

3. Claims 13-19 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Welter et al(US 4,418,069) or Dereu et al(US 4,730,053), or EP 0 366 990, or CA 02276984, or WO 9726968.

Instant claims are directed to a method for reduction of a substrate with

thioredoxin reductase, comprising combining the thioredoxin reductase, the substrate and NADPH under conditions to reduce the substrate, the substrate comprising a substance selected from the group consisting of a compound represented by the general formula (1) or (1') of claim 13 and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof. Also, claims are directed to a method of enhancing peroxidase activity of thioredoxin reductase, and method of oxidizing reduced thioredoxin by a substrate comprising combining NAPDH, thioredoxin reductase, thioredoxin and a substrate in vitro under conditions to enhance peroxidase activity of thioredoxin reductase, the substrate comprising a substance selected from the group consisting of a compound represented by the following general formula (1) or (1') and a physiologically acceptable salt thereof, and a hydrate thereof and a solvate thereof:

As explained in the previous office action, all these articles expressly teach administration of structurally similar compounds in vivo to achieve the same effect as claimed herein in-vitro. Inasmuch as the in-vivo administration is taught achieving reduction of the substrate, it is expected that in vitro effect will be achieved in the same way, absent evidence to the contrary.

4. Claims 13-19 and 26-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over combined teachings of Arteel et al(Chem. Res. Toxicol, 1999), Bjornstedt et al(JBC, 1995), and Kumar et al(Eur. J. Biochem, 1992) and in view of Muller et al(Biochem. Pharmac. 3235-3239, 1984)and Schewe (Gen. Pharmac. Vol 26, pp 1153-1169, 1995).

Arteel et al is teaching function of thioredoxin reductase as a peroxidenitrite reductase using selenocystine or ebselen in the presence of NADPH. See page 265, column 1, lines 10-17 and column 2, Fig 1, wherein in vitro experiment is expressly done using NADPH selenocystine, and thioredoxin, similar to claimed herein.

Bjornstedt et al teach that thioredoxin reductase reduces lipid hydropreoxide by NADPH and selenocystine. Thus confirming that selenium is an essential trace element to have antioxidant property. See page 11761. Also note in-vitro experiment on page 11762, column 1, wherein thioreductase is incubated with NADPH and seleno compound.

Kumar et al is expressly teaching that selenite is a substrate for thioredoxin reductase and NADPH, see the abstract and column 1, page 435, and page 437, Fig 3. The difference between the reference and herein claimed method is selenite in the reference versus ebselen claimed herein.

Muller et al is teaching that ebselen has glutathione peroxidase like antioxidant activity in vitro, see the abstract.

Finally, Schewe expressly suggest that ebselen mimics glutathione peroxidase activities, see page 1153, column 1, page 1154, column 2.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the process of Arteel et al, and Bjornstedt et al, wherein in vitro experiment is expressly done using NADPH, selenocystine and thioredoxin similar to claimed herein, by using ebselen, as taught by Muller et al and Schewe, because the latter references are expressly teaching that ebselen mimics

glutathione peroxidase like activities and Kumar et al is expressly teaching that selenite is a substrate for thioredoxin reductase and NADPH, and Bjornstedt et al is expressly teaching that selenium is an essential trace element to have anti oxidant property. Thus, given that selenium is essential element to have antioxidant property, ebselen is having glutathione peroxidase like activity in vitro, it is obvious that ebselen when reacted with thioredoxin reductase and NADPH, would result in a method similar to claimed herein, absent evidence to the contrary.

Applicants' arguments were fully considered and were not found convincing. Applicants note that, as disclosed in Bjornstedt at page 11761, right column, third full paragraph, Bjornstedt is directed to the investigation of whether thioredoxin reductase and thioredoxin can reduce lipid hydroperoxides and if low molecular weight selenium compounds could act as charge transfer catalysts. Bjornstedt discloses that this could be an important alternative pathway for the detoxification of hydroperoxides in addition to GSH-Px-mediated reduction. Thus, as noted in the rejection, Bjornstedt does not disclose methods as recited in Applicants' claims which include the recited compounds let alone teach or suggest that compounds having a structure such as ebselen would be a substrate, an inhibitor or most likely not show any reactivity.

The examiner would like to point out that Bjornstedt is expressly teaching in vitro experiment wherein NADPH, TR and selenium is reacted together, and this experiment itself renders instant method obvious because it is selenium which is important part of the reaction and other references are expressly teaching that selenium is active part, and Muller is teaching ebselen to be behaving like glutathione peroxidase

like activity, thus suggesting similar process as claimed herein. Same arguments go with Kumar reference that although, the structure is different, it is selenium that is important and the references are expressly teaching equivalence of selenite, ebselen having glutathione peroxidase like activity. Applicants argue that Arteel is not using ebselen. The examiner would like to submit same arguments as supra that it is selenium which is important and inasmuch as ebselen is taught in a similar glutathione peroxidase like activity, the method claim is obvious as a whole, absent evidence to the contrary.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAILENDRA -. KUMAR whose telephone number is (571)272-0640. The examiner can normally be reached on Mon-Thur 8:00-5:30, Alt Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571)272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHAILENDRA - KUMAR
Primary Examiner
Art Unit 1621

S.Kumar
2/19/07